

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 27373/40386	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2005/003765	International filing date (<i>day/month/year</i>) 04 February 2005 (04.02.2005)	Priority date (<i>day/month/year</i>) 06 February 2004 (06.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE UNIVERSITY OF CHICAGO		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).
 2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 07 August 2006 (07.08.2006)</p> <p>Authorized officer Dorothee Mülhausen</p> <p>e-mail: pt01@wipo.int</p>
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REC'D 20 JUN 2005

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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

17 JUN 2005

Applicant's or agent's file reference

27373/40386

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US05/03765

International filing date (day/month/year)

04 February 2005 (04.02.2005)

Priority date (day/month/year)

05 February 2004 (05.02.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 35/66; 35/00 and US CL: 424/780, 115

Applicant

UNIVERSITY OF CHICAGO

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US

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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/03765

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/03765

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 13-48	YES
	Claims 1-12	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-48	NO
Industrial applicability (IA)	Claims 1-48	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1 and 3-12 lack novelty under PCT Article 33(2) as being anticipated by Sherman et al. (US 6,096,711).

Sherman et al. teach an anti-inflammatory composition comprising one or more proteasome inhibitors in an amount sufficient to induce hsp72 production (see, for example, Abstract; column 1, line 4 - column 2, line 65; and claims including claim 8). Please note that such a composition would inherently contain one or more cytoprotective compounds therein as well as have the claimed functional effects (with respect to inducing hsp expression, inhibiting proteasome, as well as the other effects recited in claims 4-11).

Claims 1 and 3-12 lack novelty under PCT Article 33(2) as being anticipated by Madsen (Clin. Invest. Med., 2001).

Madsen teaches a composition for treating inflammatory bowel disease comprising the probiotic VSL-3 bacterial mixture and method of treating inflammatory bowel disease via administering an effective amount of VSL-3. Madsen further discloses that the VSL-3 probiotic composition inhibits epithelial cell NF-kB activation. Please note that such a composition would inherently contain one or more cytoprotective compounds therein as well as have the claimed functional effects (with respect to inducing hsp expression, inhibiting proteasome, as well as the other effects recited in claims 4-11).

Claims 1-48 lack an inventive step under PCT Article 33(3) as being obvious over Sherman et al. and Madsen.

The cited references are relied upon for the reasons set forth above. Sherman et al. also teach that numerous proteasome inhibitors may be used to induce hsp72 including those recognized by the prior art (see, for example, column 2, lines 47-65). Madsen additionally teaches that it would appear that a soluble factor is released from the VSL-3 bacterial mixture; that several mechanisms have been proposed by which probiotics may exert their beneficial activity including release of bacteriocidine and/or an organic acid such as lactic acid or butyric acid; and that the VSL-3 compound as well as conditioned medium from the VSL-3 mixture also demonstrated *in vitro* activity using the T84 human colonic epithelial cell line (see page 254, second column).

It would have been obvious to one of ordinary skill in the art to treat inflammatory conditions including inflammatory bowel disease via administering an effective amount of one of various proteasome inhibitors (such as disclosed by Sherman et al) and/or a compound obtained/isolated from the probiotic VSL-3 or from the VSL-3 conditioned medium (such as an organic acid and/or soluble factor) to a subject in need thereof based upon the beneficial teachings provided by the cited references, as discussed above. The result-effective adjustment in conventional working conditions (for example, isolating an active compound therefrom using customary extraction techniques and/or performing an assay designed to obtain/isolate an active compound therefrom) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Claims 1-48 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.